

WHAT IS CLAIMED IS:

1. A method of enhancing function of an endodermally derived organ in a subject in need thereof, the method comprising:

(a) obtaining a population of cells comprising stem and/or progenitor cells;

(b) culturing said stem and/or progenitor cells ex-vivo under conditions allowing for cell proliferation and, at the same time, culturing said cells under conditions selected from the group consisting of:

(i) conditions reducing expression and/or activity of CD38 in said cells;

(ii) conditions reducing capacity of said cells in responding to signaling pathways involving CD38 in said cells;

(iii) conditions reducing capacity of said cells in responding to retinoic acid, retinoids and/or Vitamin D in said cells;

(iv) conditions reducing capacity of said cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said cells;

(v) conditions reducing capacity of said cells in responding to signaling pathways involving PI 3-kinase;

(vi) conditions wherein said cells are cultured in the presence of

nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite;

(vii) conditions wherein said cells are cultured in the presence of a copper chelator;

(viii) conditions wherein said cells are cultured in the presence of a copper chelate;

(ix) conditions wherein said cells are cultured in the presence of a PI 3-kinase inhibitor;

thereby expanding the stem and/or progenitor cells while at the same time, substantially inhibiting differentiation of the stem and/or progenitor cells ex-vivo; and

(c) implanting said cells in an endodermally-derived organ of the subject.

2. The method of claim 1, further comprising monitoring function of said endodermally-derived organ in said subject.

3. The method of claim 1, wherein said stem and/or progenitor cells are derived from a source selected from the group consisting of hematopoietic cells, umbilical cord blood cells, G-CSF mobilized peripheral blood cells, bone marrow cells, hepatic cells, pancreatic cells, neural cells, oligodendrocyte cells, skin cells, gut cells embryonal stem cells, muscle cells, bone cells, mesenchymal cells, chondrocytes and stroma cells.

4. The method of claim 1, wherein step (b) is followed by a step comprising inducing *ex-vivo* enrichment of said stem/progenitor cells for cells having an endodermal cell phenotype.

5. The method of claim 4, wherein said inducing is effected by providing at least one hepatic growth factor and/or sodium butyrate.

6. The method of claim 5, wherein said hepatic growth factor is selected from the group consisting of FGF-1, FGF-2, LIF, OSM, HGM, FBS, HGF, EGF, and SCF.

7. The method of claim 1, further comprising the step of selecting a population of stem cells enriched for hematopoietic stem cells.

8. The method of claim 7, wherein said selection is affected via CD34.

9. The method of claim 1, further comprising the step of selecting a population of stem cells enriched for early hematopoietic stem/progenitor cells.

10. The method of claim 9, wherein said selection is affected via CD133.

11. The method of claim 1, wherein step (b) is followed by a step comprising selection of stem and/or progenitor cells.

12. The method of claim 11, wherein said selection is affected via CD 133 or CD 34.

13. The method of claim 1, wherein said endodermally-derived organ is a liver, an intestine or a pancreas.

14. The method of claim 1, wherein said providing said conditions for cell proliferation is effected by providing the cells with nutrients and cytokines.

15. The method of claim 14, wherein said cytokines are selected from the group consisting of early acting cytokines and late acting cytokines.

16. The method of claim 15, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.

17. The method of claim 12, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.

18. The method of claim 12, wherein said late acting cytokine is granulocyte colony stimulating factor.

19. The method of claim 1, wherein said subject is a human.

20. The method of claim 1, wherein said stem and/or progenitor cells are genetically modified cells.

21. The method of claim 1, wherein said stem and/or progenitor cells are derived from said subject.

22. The method of claim 1, wherein said inhibitors of PI 3-kinase are wortmannin and/or LY294002.

23. The method of claim 1, wherein step (b) further comprises co-culturing said stem and/or progenitor cells with endodermally-derived organ tissue.

24. A method of expanding and transdifferentiating a population of non-endodermally derived stem cells into stem cells having an endodermal cell phenotype, the method comprising:

(a) obtaining a population of cells comprising stem and/or progenitor cells;

(b) culturing said stem and/or progenitor cells ex-vivo under conditions allowing for cell proliferation and, at the same time, culturing said cells under conditions selected from the group consisting of:

(i) conditions reducing expression and/or activity of CD38 in said cells;

(ii) conditions reducing capacity of said cells in responding to signaling pathways involving CD38 in said cells;

(iii) conditions reducing capacity of said cells in responding to retinoic acid, retinoids and/or Vitamin D in said cells;

(iv) conditions reducing capacity of said cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said cells;

(v) conditions reducing capacity of said cells in responding to signaling pathways involving PI 3-kinase;

(vi) conditions wherein said cells are cultured in the presence of

nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite;

(vii) conditions wherein said cells are cultured in the presence of a copper chelator;

(viii) conditions wherein said cells are cultured in the presence of a copper chelate;

- (ix) conditions wherein said cells are cultured in the presence of a PI 3-kinase inhibitor; thereby expanding the stem and/or progenitor cells while at the same time, substantially inhibiting differentiation of the stem and/or progenitor cells ex-vivo; and
- (c) inducing enrichment of said stem/progenitor cells for stem cells expressing endodermal cell markers, thereby expanding and transdifferentiating a population of non-endodermal stem cells into stem cells having an endodermal cell phenotype.

25. The method of claim 24, wherein said stem and/or progenitor cells are derived from a source selected from the group consisting of hematopoietic cells, umbilical cord blood cells, G-CSF mobilized peripheral blood cells, bone marrow cells, neural cells, oligodendrocyte cells, skin cells, **gut cells**, embryonal stem cells, muscle cells, bone cells, mesenchymal cells, chondrocytes and stroma cells.

26. The method of claim 24, wherein said inducing is effected by providing at least one hepatic growth factor and/or sodium butyrate.

27. The method of claim 26, wherein said hepatic growth factor is selected from the group consisting of FGF-1, FGF-2, LIF, OSM, HGM, FBS, HGF, EGF, and SCF.

28. The method of claim 24, further comprising the step of selecting a population of stem cells enriched for hematopoietic stem cells.

29. The method of claim 28, wherein said selection is affected via CD34.

30. The method of claim 24, further comprising the step of selecting a population of stem cells enriched for early hematopoietic stem/progenitor cells.

31. The method of claim 30, wherein said selection is affected via CD133.

32. The method of claim 24, wherein step (b) is followed by a step comprising selection of stem and/or progenitor cells.

33. The method of claim 32, wherein said selection is affected via CD 133 or CD 34.

34. The method of claim 24, wherein said providing said conditions for cell proliferation is effected by providing the cells with nutrients and cytokines.

35. The method of claim 34, wherein said cytokines are selected from the group consisting of early acting cytokines and late acting cytokines.

36. The method of claim 35, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.

37. The method of claim 35, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.

38. The method of claim 37, wherein said late acting cytokine is granulocyte colony stimulating factor.

39. The method of claim 24, wherein said stem and/or progenitor cells are genetically modified cells.

40. The method of claim 24, wherein said endodermal cell markers are selected from the group consisting of insulin, glucagon, somatostatin, pancreatic polypeptide, Pdx-1, pancreatic enzymes, C-peptide, albumin, CK18, CK 19, HNF, THY-1 receptor, c-Met receptor and c-kit.

41. The method of claim 24, wherein step (b) further comprises co-culturing said stem and/or progenitor cells with endodermally-derived organ tissue.

42. A therapeutic *ex vivo* cultured stem cell population comprising non-endodermally-derived cells expanded and transdifferentiated according to the methods of any of claims 24-41.

43. The cell population of claim 42, in a culture medium comprising at least one hepatic growth factor and/or sodium butyrate.

44. The cell population of claim 42, isolated from said medium.

45. A pharmaceutical composition comprising the cell population of claim 43 and a pharmaceutically acceptable carrier.

46. A pharmaceutical composition comprising the cell population of claim 44 and a pharmaceutically acceptable carrier.

47. A method of producing an endocrine hormone comprising the method of claim 24, and further comprising the step of continuing to culture said transdifferentiated cells in said medium, whereby an endocrine hormone may be produced.

48. The method of claim 47, wherein said endocrine hormone is selected from the group consisting of insulin, glucagon and somatostatin.

49. The endocrine hormones produced by the method of claim 47.

50. The method of claim 1, used for treating or preventing a liver or pancreatic disease.

51. The method of claim 50, wherein said liver disease is selected from the group consisting of primary biliary cirrhosis, hepatic cancer, primary sclerosing cholangitis, autoimmune chronic hepatitis, alcoholic liver disease, infectious hepatitis, parasitic hepatic disease, steatohepatitis and hepatic toxicity.

52. The method of claim 50, wherein said pancreatic disease is selected from the group consisting of acute pancreatitis, chronic pancreatitis, hereditary pancreatitis, pancreatic cancer, diabetes.